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A New Stereoselective Synthesis of Chiral γ-Functionalized (*E*)-Allylic Amines

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Abstract: Chiral *t*-Boc protected propargylic amines have been obtained starting from aminoaldehydes derived from natural aminoacids. Stannylcupration of these substrates affords an easy regio- and stereocontrolled route to the corresponding γ-stannylated (*E*)-allylamines which are useful intermediates for the synthesis of the corresponding γ-funtionalized allylic systems.
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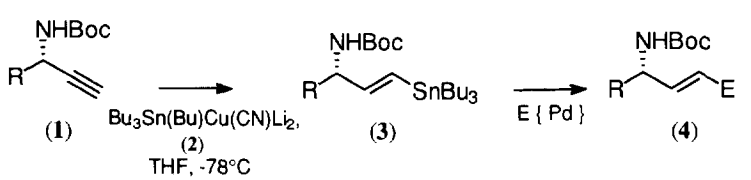
INTRODUCTION

Chiral *trans*-allylic amines are synthetically[1] and biologically[2] relevant, not only for their therapeutic properties but also because they have proven to be useful intermediates, for example, in the synthesis of conformationally restricted peptide isosteres.[3] Therefore, several methods have recently been developed to stereoselectively obtain these kind of compounds, based either on the control of asymmetric induction[4] in the new C-C bond formed, or by functional group transformation of a suitable precursor.[3a,5] In particular it was reported[5a] that chiral propargylic amines, obtained with high enantiomeric purity from naturally occurring amino acids, are appropriate intermediates for this purpose.

During our studies on the addition reaction of mixed stannylcuprates on γ-substituted alkynes, we showed[6] that suitably protected propargylamines may act as substrates to afford highly functionalized allylic systems. These were achieved *via* the intermediate N-(*t*-Boc)-(*E*)-1-amino-3-tributylstannyl-prop-2-ene (**3** when R=H) which proved to be a useful three-carbon homologating reagent, the vinyl-tin moiety being able to react with electrophiles *via* palladium catalysed coupling.[7]



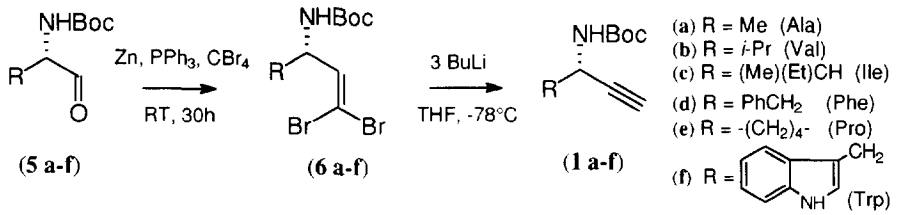
Scheme 1

As both the reaction steps take place under very mild conditions and are tolerant of a wide variety of functionalities, we thought that the extension of such a reaction sequence to a range of chiral propargylic amines (**1**) could proceed without racemization thus constituting a new stereocontrolled procedure to chiral allylic amines (Scheme 1).

In the present paper we wish to report our results on the stereoselective synthesis of a range of chiral protected α-substituted-γ-stannylated (*E*)-allylic amines (**3**) whose reactivity has been investigated aimed at the synthesis of the corresponding γ-functionalized compounds (**4**). With this goal in mind we also investigated an efficient route to the synthesis of the propargylic precursors (**1**) that will be discussed in detail.

RESULTS AND DISCUSSION

The first problem we had to face was the choice of an efficient stereoselective synthesis for substrates of type (**1**). Despite their synthetic interest,[8] there is a lack of general methods for the synthesis of such compounds. Although most of them proceed through the amination of propargylic substrates,[9] an efficient method has recently been reported to convert chiral aminoaldehydes to the corresponding propargylamine in one step by exposure to dimethyldiazophosphonate.[5a] As the transformation of naturally occurring aminoacids to the corresponding aldehydes is a very well known procedure[10] and there are several examples available for the aldehyde-to-alkyne[11] homologation, we envisaged using a similar approach to develop a new synthetic pathway for achieving compounds of type (**1**). Therefore, following the well known procedure originally developed by McKelvie[12] and later extended by Corey and Fuchs,[13] we decided to transform aldehydes (**5 a-f**) to the corresponding 3,3-dibromo alkenes (**6 a-f**) from which it should be possible to obtain the alkyne derivatives (**1 a-f**) by simple treatment with BuLi at low temperature[13] (Scheme 2):



Scheme 2

Indeed this reaction sequence has already been applied to the synthesis of compound (**1e**) starting from (*L*)-N-Boc-prolinal (**5e**), showing that the tranformation occurs without racemization at the stereogenic center.[14] This fact, coupled with the consideration that intermediates (**6**) are by themeselves useful chiral building blocks,[15] prompted us to choose this reaction sequence for the synthesis of substrates (**1**).

Dibromo-ethylene triphenylphosphorane was prepared as reported,[13] and reacted with aldehydes (**5 a-f**) at room temperature. After completion the reaction mixture was diluted with pentane and the residue filtered: the expected dibromo derivatives (**6 a-f**) were then isolated by simple filtration over a SiO_2 plug.

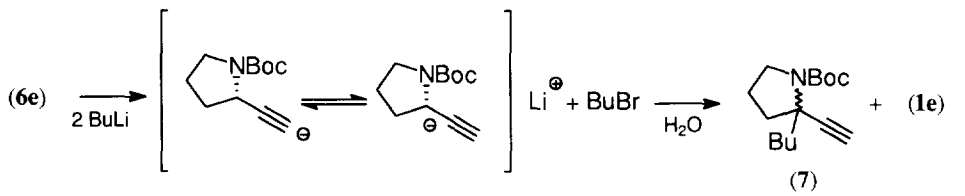
Our results are reported in Table 1. Compounds (**6a-f**) were always isolated in reasonable yields, however, in the case of (**6f**), a modified procedure[16] recently reported to be more suitable for sensitive aldehydes, had to be used in order to gain similar results. Conversion of dibromides (**6a-f**) into the corresponding propargylic amines was then performed in the presence of 3 equivalents of BuLi at low temperature. The reaction proceeded smoothly and afforded, as expected, compounds (**1 a-f**) in high yields, as shown in Table 1.

Table 1. Yields and $[\alpha]_D$ Values Determined for Compounds (**6a-f**) and (**1a-f**)

Starting material	(**6**)[a]	$[\alpha]_D$	(**1**)[a]	$[\alpha]_D$
(**5a**)	(**6a**) 51%	$[\alpha]^{21}_D$=+20.5 *c*=0.99 $CHCl_3$	(**1a**) 70% (67%)[b]	$[\alpha]^{21}_D$=-61.5[5a] *c*=1.01 $CHCl_3$
(**5b**)	(**6b**) 72%	$[\alpha]^{24}_D$=+25.3 *c*=1.01 $CHCl_3$	(**1b**) 83%	$[\alpha]^{22}_D$=-45.3[5a] *c*=1.04 $CHCl_3$
(**5c**)	(**6c**) 64%	$[\alpha]^{21}_D$=-21.9 *c*=1.00 $CHCl_3$	(**1c**) 94%[c]	$[\alpha]^{20}_D$=-32.2 *c*=1.01 $CHCl_3$
(**5d**)	(**6d**) 73%	$[\alpha]^{21}_D$=+39.9 *c*=1.01 $CHCl_3$	(**1d**) 88%	$[\alpha]^{21}_D$=-10.6[5a] *c*=1.01 $CHCl_3$
(**5e**)	(**6e**) 62%	$[\alpha]^{21}_D$=+30.6[14] *c*=1.04 $CHCl_3$	(**1e**) 42%	$[\alpha]^{21}_D$=-67.3[14] *c*=0.67 $CHCl_3$
(**5f**)	(**6f**) 68%	$[\alpha]^{21}_D$=+6.2 *c*=1.08 $CHCl_3$	(**1f**) 89%	$[\alpha]^{21}_D$=+4.2 *c*=1.08 $CHCl_3$

a) Yield of isolated compounds
b) Overall yield without isolation of the intermediate (**6a**)
c) Calculated on the crude by ^1H NMR analysis

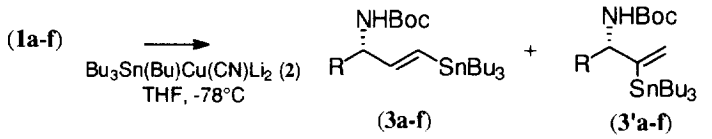
All the chiral propargylic amines obtained were isolated and fully characterized and the observed $[\alpha]_D$ values were in good agreement with those previously reported for compounds (**1a,b,d,e**).[5a,14] It has also to be pointed out that the whole transformation from (**5**) to (**1**) can be carried out without isolation of the intermediate (**6**) as we checked for compound (**1a**) which was isolated in a 67% overall yield.



Scheme 3

Only in the case of (**1e**) was a low yield observed and a relevant amount of by-product identified as (**7**) was isolated from the crude mixture (Scheme 3). Remarkably a similar behaviour, which has been already noted[14] for this substrate, was not generalized to all the other cases which we examined: an enhancement of the acidity of the proton on the stereogenic center on (**1e**) could be expected, due to the presence of the pyrrolidinic ring.[17]

The reactivity of propargylamines (**1 a-f**) towards additon of the H. O. mixed stannylcuprate (**2**) was then investigated (Scheme 4). Reagent (**2**) was prepared as reported[18] and the substrate added at -78° C. As we already observed in the case of N-(*t*-Boc)-propargylamine,[6a] the reaction occurred at appreciable rates, under very mild conditions, with complete conversion of our substrates into the γ-substituted tributylstannylderivatives (**3a-f/3'a-f**). The regioisomeric ratio was detemined by ^{1}H-NMR analysis of the crude after quenching the reaction mixture with ammonic buffer at low temperature.



Scheme 4

The *trans* geometry of the compounds (**3a-f**) was easily assigned by measuring the coupling constants of the ethylenic protons which were, in all cases, in agreement with those previously found for a similar compound.[6a] Detailed results are reported in Table 2.

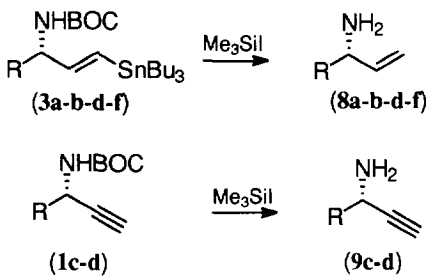
Table 2. Experimental Details for Stannylated Allylamines (**3a-f**)

Product (yield) [a]	(**3a**) 73%	(**3b**) 73%	(**3c**) 59%	(**3d**) 88%	(**3e**) 58%	(**3f**) 69%
(**3/3'**)[b]	>95/5	90/10	95/5	>95/5	90/10	90/10
$[\alpha]_D$[c]	$[\alpha]^{25}_D$=-29.9 *c*=0.98 $CHCl_3$	$[\alpha]^{25}_D$=-14.5 *c*=1.04 $CHCl_3$	$[\alpha]^{20}_D$=-11.2 *c*=1.02 $CHCl_3$	$[\alpha]^{20}_D$=-5.9 *c*=1.00 $CHCl_3$	$[\alpha]^{20}_D$=-50.5 *c*=0.61 $CHCl_3$	$[\alpha]^{25}_D$=-2.8 *c*=1.15 $CHCl_3$
J Hz	19.0	19.1	18.9	19.0	19.0	19.2

a) Yield of isolated compounds
b) Determined by ^{1}H NMR analysis of the crude
c) Referred to pure **3**

As shown the presence of a lateral chain in the α position to the amino group does not affect the regioselectivity of the addition reaction, the desired compounds (**3a-f**) having been obtained regio- and stereoselectively and isolated in good yields.

The enantiomeric purity of compounds (**3a**), (**3b**), (**3d**), (**3f**), (**1c**) and (**1d**) was established by ^{1}H NMR analysis of the diastereomeric Mosher amides prepared by reaction of (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPACl) with the primary amines (**8a**), (**8b**), (**8d**), (**8f**) and (**9c**), (**9d**), in turn obtained by removal of the Boc protective group in presence of Me_3SiI.[19] It has to be noted that compounds (**3a**), (**3b**), (**3d**) and (**3f**) were completely destannylated under these reaction conditions (Scheme 5). The observed enantiomeric excesses are reported in Table 3



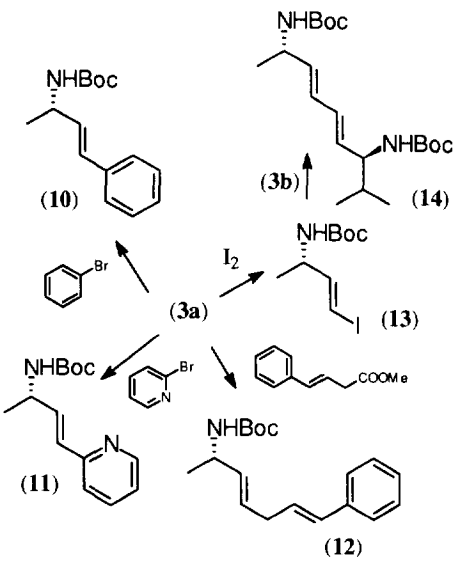
Scheme 5

Table 3.Enantiomeric Excesses Determined by Mosher Method

Starting material	(8)	e.e	(9)	e.e
(3a)	(8a)	98%		-
(3b)	(8b)	94%		-
(1c)	-	-	(9c)	93%
(1d),(3d)	(8d)	92%	(9d)	93%
(3f)	(8f)	27%		

As the enantiomeric excess observed for compounds (**8d**) and (**9d**) was the same, we assumed that during the addition of (**2**) no racemization occurred in our reaction conditions. The low enantiomeric excess of (**8f**) is probably due to a high extent of racemization occurring in the aldehyde-to-alkyne homologation step.

As a further step we investigated the reactivity of the vinyltin moiety towards different electrophiles (Scheme 6). Compound (**3a**) was chosen as model substrate and was allowed to react with aryl and vinyl halides or allyl acetate under Pd complexes catalysis, following the well known Stille procedure.[7] Experimental details, together with the obtained resuls are reported in Table 4.



Scheme 6

Table 4. Experimental Details for the Coupling Reactions on Stannylated Allylamines.

Product (Yield)[a]	Reaction cond.	$[\alpha]_D$	e.e[b]
(**10**) (63%)	$Pd(PPh_3)_4$ C_6H_6, 80 °C, 48h	$[\alpha]^{22}_D$=-60.9 *c*=1.08 $CHCl_3$	98%
(**11**) (60%)	$Pd(PPh_3)_4$ C_6H_6, 80 °C, 40h	$[\alpha]^{24}_D$=-60.9 *c*=1.12 $CHCl_3$	98%
(**12**) 68%)	LiCl,$Pd_2(dba)_3$ (3%) DMF, R.T., 24 h	$[\alpha]^{20}_D$=-30.6 *c*=1.05 $CHCl_3$	98%
(**13**) (71%)	$CHCl_3$, R.T., 3h	$[\alpha]^{22}_D$=-55.3 *c*=1.02 $CHCl_3$	98%
(**14**) (54%)	$PdCl_2(CH_3CN)_2$ (10%) DMF, R.T., 50h	$[\alpha]^{24}_D$=-25.7 *c*=1.08 $CHCl_3$	94%

a) Yield of isolated compounds

b) Assuming that no racemization occurred in the coupling reaction[21]

The expected coupling products (**10-14**) were always obtained and isolated with reasonable yields. Iododestannylation was also carried out simply by treating (**3a**) with iodine at room temperature and afforded compound (**13**) which was subsequently used as the electrophile in the reaction with (**3b**), thus achieving the

coupling of two different allylamine framework (**14**). This particular two-step transformation shows how the presence of a vinylstannyl moiety makes possible a tuning of reactivity at position 3 of the allylamine backbone thus allowing selection of the polarity of this carbon according to a particular synthetic need. It has also to be pointed out that, due to the great difference in reactivity of (**3**) and (**3'**),[20,6a] fairly clean compounds can been obtained even starting with a mixture of the vinyltin precursors.

^{1}H-NMR analysis showed that, as expected, all the final cross-coupled products were obtained with retention of configuration of the double bond in the starting material. As the enantiomeric excess proved not to be altered in the reaction conditions used,[21] we can conclude that we have shown in this paper a general and enantioselective four-step route to γ-functionalized (*E*) chiral allylic amines starting from aminoaldehydes, which features a total control of the double bond geometry.

EXPERIMENTAL SECTION

General methods.

Air and moisture sensitive compounds were protected by and handled under an atmosphere of 99.99% pure nitrogen. *Ethereal extracts were dried* with sodium sulfate. The temperature of dry ice-ethanol baths is -78°C, that of ice-sodium chloride as -15° C, that of ice as 0° C and "room temperature" as 25° C. Purifications by *flash column chromatography*[22] were performed using glass columns (10-50 mm wide); silica gel 230-400 mesh was chosen as the stationary phase (15 cm high), with an elution rate of 5 cm/min. *Nuclear magnetic resonance spectra* of hydrogen nuclei were recorded at 200 or 300 MHz. Chemical shifts were determined relative to the residual solvent peak ($CHCl_3$: 7.26 ppm). Coupling constants (*J*) are measured in Hz. Coupling patterns are described by abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of a doublet), m (multiplet), bs (broad singlet). Nuclear magnetic resonance spectra of carbon -13 nuclei were recorded at 50.3 MHz. Chemical shifts were determined relative to the residual solvent peak ($CHCl_3$: 77.0 ppm). In the case of the Mosher amides the enantiomeric excess has been determined by calculating the integral ratio of the protons of the methoxyl groups of the diastereomers obtained. In these cases only the chemical shifts of those diagnostic signals are reported. *Mass spectra* were obtained at a 70 eV ionization potential, organotin fragments are given for ^{120}Sn. *Polarimetric measurements* were performed in $CHCl_3$ solution at l = 589 nm, and the temperature is specified case by case. *IR spectra* were recorded in CCl_4 solution.

Materials. Chiral aldehydes were prepared according to a literature procedure[23] and used immediately. *Starting materials* are commercially available unless otherwise stated. All commercial reagents were used without further purification. *THF* and *diethyl ether* were obtained anhydrous by distillation over sodium wire and subsequent double distillation over $LiAlH_4$. *Methylene chloride* was purified by the standard procedure, dried over calcium chloride and stored over 4-Å molecular sieves. *Benzene* was distilled over sodium wires and stored over 4-Å molecular sieves. *DMF* was distilled over calcium hydride and stored over 4-Å molecular sieves. *Petroleum ether*, unless specified, is the 40-70°C boiling fraction.

Synthesis of α-substituted (S)-N-(t-butoxycarbonyl)-3,3-dibromo-2-propenamines (**6**). *General procedure.*

Powdered Zn (2 eq.), PPh_3 (2 eq.) and CBr_4 (2 eq.), were mixed together, then dissolved in CH_2Cl_2 and left to react overnight under an inert atmosphere.[13] 1 equivalent of freshly prepared chiral aldehyde (**5**) was dissolved in CH_2Cl_2 and added to the reagent. After 16 hours stirring the mixture was diluted with pentane, the resulting black residue filtered, the solvent evaporated and the crude product eluted on SiO_2.

(S)-1-Methyl-3,3-dibromo-N-(t-butoxycarbonyl)-2-propenamine (**6a**)

565 mg (3.3 mmol) of (S)-aldehyde (**5a**) were reacted according to the general procedure. The crude product afforded, after chromatography (eluent: petroleum ether/ethyl acetate = 5/2) 546 mg (1.7 mmol) of pure (**6a**) (yield 51%) as a pale yellow oil. (**6a**): ^{1}H-NMR (200 MHz) δ: 6.34 [d, 1H, *J* = 8.2 Hz]; 4.6-4.4 [m, 1H];

4.38 [m, 1H]; 1.45 [s, 9H]; 1.25 [d, 3H, *J* = 6.7 Hz]. ^{13}C-NMR (50.3 MHz) δ: 155.3; 141.0; 90.5; 80.4; 50.1; 28.9; 20.3. MS *m/e*: 215/213/211 (4/11/5); 194/192 (40/40); 148 (9); 133/131 (6/6); 88 (6); 59 (24); 57(100). $[\alpha]^{21}_D$ = + 20.5 (*c* = 0.99, $CHCl_3$). Anal. Calcd for $C_9H_{15}Br_2NO_2$: C, 32.85; H, 4.60; N, 4.26. Found: C, 32.97; H, 4.62; N, 4.28.

(S)-1-(1'-methyl)-ethyl-3,3-dibromo-N-(t-butoxycarbonyl)-2-propenamine (**6b**)

2.120 g (10.5 mmol) of (S)-aldehyde (**5b**) were reacted following the general procedure. 4.230 g of crude mixture were obtained and analyzed by ^{1}H-NMR. Compound (**6b**) and triphenylphosphine oxide were present in 5:1 ratio. 420 mg of the crude mixture were filtered over SiO_2 (eluent CH_2Cl_2) affording 268 mg (0.75 mmol) of pure (**6b**) (72%) as a white solid. (**6b**): mp = 73-74° C. ^{1}H-NMR (200 MHz) δ: 6.29 [d, 1H, *J* = 9.2 Hz]; 4.56 [d, 1H, *J* = 7.2Hz]; 4.2-4.0 [m, 1H]; 1.92-1.72 [m, 1H]; 1.44 [s, 9H]; 0.94 [d, 3H, *J* = 7.0 Hz]; 0.95 [d, 3H, *J* = 7.0 Hz]. ^{13}C-NMR (50.3 MHz) δ: 155.1; 137.9; 91.4; 79.7; 58.4; 32.1; 28.6; 18.5; 18.3. MS *m/e*: 316/314/312 (5/9/7); 303/301/299 (4/8/6); 260/258/256 (44/100/60); 243/241/239 (5/13/8); 178 (29); 85 (43); 83 (69); 79 (21); 59 (80); 57 (100). $[\alpha]^{24}_D$ = + 25.3 (*c* = 1.01, $CHCl_3$). Anal. Calcd. for $C_{11}H_{19}Br_2NO_2$: C, 37.00; H, 5.36; N, 3.92. Found: C, 37.12 H, 5.39 N, 3.90

(S)-1-(1'-methyl)-propyl-3,3-dibromo-N-(t-butoxycarbonyl)-2-propenamine (**6c**)

751 mg (3.5 mmol) of (S)-aldehyde (**5c**) were reacted according to the general procedure. 1.122 g of crude mixture were obtained and filtered over SiO_2 (eluent CH_2Cl_2) to afford 835 mg (2.25 mmol) of pure (**6c**) (64%) as a white low melting solid. (**6c**): ^{1}H-NMR (300 MHz) δ: 6.29 [d, 1H, *J* = 9.3 Hz]; 4.7-4.4 [m, 1H]; 4.3-4.0 [m, 1H]; 1.7-1.5 [m, 1H]; 1.44 [s, 9H]; 1.3-1.1 [m, 2H]; 1.0-0.9 [m, 3H + 3H]. ^{13}C-NMR (75.45 MHz) δ: 155.4; 138.2; 92.0; 80.0; 58.0; 39.5; 29.0; 25.8; 15.3; 12.0. MS *m/e*: 315 (1); 316/314/312 (2/4/1); 260/258/256 (17/32/18); 216/214/212 (4/12/5); 59 (24); 57 (100). $[\alpha]^{21}_D$ = -21.9 (*c* = 1.00, $CHCl_3$). Anal. Calcd for $C_{12}H_{21}Br_2NO_2$: C, 38.84; H, 5.70; N, 3.77. Found: C, 38.75; H, 5.67; N, 3.79.

(S) 1-benzyl-3,3-dibromo-N-(t-butoxycarbonyl)-2-propenamine (**6d**)

2.470 g (9.9 mmol) of (S)-aldehyde (**5d**) were reacted according to the general procedure. 6.215 g of crude mixture were obtained, which after filtration over SiO_2 (eluent CH_2Cl_2) afforded 2.927 g (7.2 mmol) of pure (**6d**) (73%) as a white solid. (**6d**): mp = 127-129° C. ^{1}H-NMR (300 MHz) δ: 7.3-7.2 [m, 3H]; 7.2-7.1 [m, 2H]; 6.38 [d, 1H, *J* = 8.1 Hz]; 4.6-4.4 [m, 1H + 1H]; 2.89 [d, 2H, *J* = 5.1 Hz]; 1.41 [s, 9H]. ^{13}C-NMR (75.45 MHz) (APT) δ: 154.8; 138.5; 136.3; 129.5; 128.5; 126.8; 91.0; 79.9; 55.7; 39.8; 28.3. MS *m/e*: 316/314/312 (5/9/4); 260/258/256 (20/39/21); 216/214/212 (19/36/22); 128(41); 92 (37); 91 (46); 86 (11); 84 (15); 65 (24); 59 (15); 57 (100). $[\alpha]^{21}_D$ = + 39.9 (*c* = 1.01, $CHCl_3$). Anal. Calcd. for $C_{15}H_{19}Br_2NO_2$: C 44.47; H 4.73; N 3.46. Found: C 44.65; H 4.75; N 3.44.

(S)-1-α-pyrrolidin-3,3-dibromo-N-(t-butoxycarbonyl)-2-propenamine (**6e**)

368 mg (1.8 mmol) of (S)-aldehyde (**5e**) were reacted according to the general procedure. 786 mg of crude mixture were obtained which after filtration over SiO_2 (eluent CH_2Cl_2) afforded 394 mg (1.1 mmol) of pure (**6e**) (62%) as a white solid. (**6e**): mp = 67-69°C[14]. ^{1}H-NMR (200 MHz) δ: 6.34 [d, 1H, *J* = 8.1 Hz]; 4.36 [m, 1H]; 3.4-3.3 [m, 2H]; 2.2-2.0 [m, 1H]; 1.9-1.6 [m, 2H + 1H] 1.4 (s, 9H). ^{13}C-NMR (75.45 MHz) δ: 154.2; 140.3; 88.2; 79.7; 59.4; 46.4; 31.7; 28.4; 23.6. MS *m/e*: 301/299/297 (1/3/1); 218/220 (42/42); 201/199/197 (4/9/3); 176/174(15/15); 91 (55); 84 (61); 69 (22); 57 (100). $[\alpha]^{19}_D$ = + 30.6 (*c* = 1.04, $CHCl_3$). Anal. Calcd. for $C_{11}H_{17}Br_2NO_2$: C 37.21; H 4.83; N 3.94. Found: C, 37.16; H, 4.85; N, 3.92.

(S)-1-[methyl-(3'-indolyl)]-3,3-dibromo-N-(t-butoxycarbonyl)-2-propenamine (**6f**)

2.533 g (7.6 mmol) of CBr_4 were dissolved in 50 ml of CH_2Cl_2 and cooled at -20°C, then a solution of 2.040 g (7.8 mmol) of PPh_3 in CH_2Cl_2 (100 mL) was added and left to react for 30 min. After cooling to -60°C, a mixture of 1.096 g (3.8 mmol) of (**5f**) and 0.53 ml (3.8 mmol) of NEt_3 in CH_2Cl_2 (20 mL), was slowly added and stirred for 30 min at -60° C. The reaction mixture was then heated at room temperature and left for further 30 min. After this time it was diluted with petroleum ether (150 mL) then filtered. Evaporation of the solvent afforded 2.162 g of crude. 1.080 g of the crude were purified by flash chromatography (eluent: petroleum ether/ethyl acetate = 2/1) affording 562 mg (1.3 mmol) of (**6f**) as a pale brown solid.(yield: 68%). (**6f**): mp = 129-132°C. ^{1}H-NMR (200 MHz) δ: 8.36 [bs, 1H]; 7.62 [bd, 1H, *J* = 8.0 Hz]; 7.37 [d, 1H, *J* = 8.0 Hz]; 7.26-

7.10 [m, 2H]; 7.05 [bs, 1H]; 6.40 [d, 1H, *J* = 6.9 Hz]; 4.8-4.5 [m, 1H + 1H]; 3.07 [m, 2H]; 1.43 [s, 9H]. ^{13}C-NMR (50.3 MHz) δ: 155.0; 139.5; 136.3; 127.5; 123.1; 122.1; 119.6; 118.9; 111.2; 110.1; 90.3; 79.9; 53.7; 29.4; 28.3. MS *m/e*: 444 (0.03); 371 (0.25); 131 (13); 130 (100); 57 (34). $[\alpha]^{21}_D$ = + 6.2 (*c* = 1.08, $CHCl_3$). Anal. Calcd. for $C_{17}H_{20}Br_2N_2O_2$: C 45.97; H 4.54; N 6.31. Found: C, 45.88; H, 4.51; N, 6.29.

Synthesis of a-substituted (S)-N-(t-butoxycarbonyl)-2-propynamine (**1**). *General procedure.*

1 eq. of (**6**) was dissolved in THF and cooled at -78°C. 3 eq. of BuLi were added, left to react, with stirring for 1 hour and then warmed to room temperature. The reaction mixture was left to react until TLC analysis showed the starting aldehyde had disappeared, then cooled again at -78°C, hydrolyzed with 0.01 M NaOH and extracted with ether. The organic phase was washed with brine twice, the solvent evaporated and the obtained crude mixture purified by flash chromatography.

(S)-1-methyl-N-(t-butoxycarbonyl)-2-propynamine (**1a**)

328 mg (1.0 mmol) of (**6a**) were reacted following the general procedure for 1 hour. After work-up, 315 mg of crude product were obtained which after purification (eluent: CH_2Cl_2) afforded 118 mg (0.70 mmol) of pure (**1a**) as a white, low melting solid (yield 70%). (**1a**): ^{1}H-NMR (200 MHz) δ: 4.7-4.6 [m, 1H]; 4.6-4.4 [m, 1H]; 2.26 [d, 1H, *J* = 2.2 Hz];.1.44 [s, 9H]; 1.40 [d, 3H, *J* = 4.4 Hz]. ^{13}C-NMR (75.45 MHz) δ: 155.5; 92.0; 80.3; 70.1; 38.9; 28.8; 23. MS *m/e*: 154 (5); 113 (61); 98 (11); 59 (53); 57 (100). IR (CCl_4): 3457; 3312 (ν C≡**C-H**); 1720. $[\alpha]^{21}_D$ = - 61.5 (*c* = 1.01, $CHCl_3$). Anal. Calcd. for $C_9H_{15}NO_2$: C, 63.88; H, 8.93; N, 8.28. Found: C, 63.94 ; H, 8.96; N, 8.31.

(S)-1-(1'-methyl)-ethyl-N-(t-butoxycarbonyl)-2-propynamine (**1b**)

1.450 g (4.1 mmol) of (**6b**) were reacted following the general procedure at -78° C for 1 hour. After workup 2.051 g of crude product were obtained which after purification (eluent: petroleum ether/ethyl acetate = 2/1) afforded 681 mg (3.4 mmol) of pure (**1b**) as a white solid (yield 83%). (**1b**): m.p.= 60-61° C. ^{1}H-NMR (200 MHz) δ: 4.8-4.6 [m, 1H]; 4.4-4.2 [m, 1H]; 2.25 [d, 1H, *J* = 2.6 Hz];.1.90 [m, 1H] 1.45 [s, 9H]; 0.98 [d, 6H, *J* = 6.6 Hz]. ^{13}C-NMR (75.45 MHz) δ: 154.8; 81.9; 79.6; 71.6; 48.4; 32.8; 28.2; 18.5;17.4. MS *m/e*: 154 (2); 141 (2); 130 (12); 116 (44); 97 (12); 95 (12); 72 (36); 71 (13); 69 (19); 57 (100). IR (CCl_4): 3459; 3313 (ν C≡**C-H**); 1719. $[\alpha]^{22}_D$= - 45.3 (*c* = 1.04, $CHCl_3$). Anal.Calcd. for $C_{11}H_{19}NO_2$: C 66.97; H 9.71; N 7.10. Found: C 67.13; H 9.67, N 7.06.

(S)-1-(1'-methyl)-propyl-N-(t-butoxycarbonyl)-2-propynamine (**1c**)

637 mg (1.7 mmol) of (**6c**) were reacted following the general procedure for 2 hours at -78°C. After workup 345 mg (1.6 mmol) of (**1c**) were obtained (yield 94%). Kugel-Rohr distillation afforded a pure sample of (**1c**) as a colourless oil. (**1c**): ^{1}H-NMR (200 MHz) δ: 4.8-4.7 [m, 1H]; 4.5-4.3 [m, 1H]; 2.23 [d, 1H, *J* = 2.6 Hz];.1.7-1.5 [m, 1H]; 1.44 [s, 9H]; 1.4-1.1 [m, 2H]; 0.95 [d, 3H, *J* = 6.6 Hz]; 0.92 [t, 3H, *J* = 7.3 Hz]. ^{13}C-NMR (75.45 MHz) (APT) δ: 154.8; 81.7; 79.8; 71.9; 47.3; 39.2; 28.3; 26.0; 14.3; 11.5. MS *m/e*: 155 (4); 154 (23); 99 (6); 59 (21); 57 (100); 54 (59). IR (CCl_4): 3463; 3313 (ν C≡**C-H**); 1708. $[\alpha]^{20}_D$ = - 32.2 (*c* = 1.01, $CHCl_3$) Anal.Calcd for $C_{12}H_{21}NO_2$: C 68.28; H 10.02; N 6.63. Found: C, 68.21; H, 10.00; N, 6.64.

(S)-1-benzyl-N-(t-butoxycarbonyl)-2-propynamine (**1d**)

2.635 g (6.5 mmol) of (**6d**) were reacted following the general procedure for 2 hours at -78°C. After workup 1.666 g of crude were obtained. 304 mg of the crude were purified by column chromatography (Florisil, eluent: petroleum ether/ethyl acetate = 3/1) to afford 257 mg (1.0 mmol) of pure (**1d**) as a pale yellow solid (yield 88%).(**1d**): m.p.= 84-87°C. ^{1}H-NMR (200 MHz) δ: 7.3-7.2 [m, 5H]; 4.7-4.6 [m, 1H+1H]; 3.02 [dd, 1H, *J* = 11.8 Hz, *J* = 5.6 Hz]; 2.94 [dd, 1H, *J* = 11.8 Hz, *J* = 4.6 Hz]; 2.28 [m, 1H]; 1.43 [s, 9H]. ^{13}C-NMR (50.3 MHz) (APT) δ: 154.5; 136.3; 129.8, 128.3, 126.9; 82.8; 80.4; 72.1; 42.8; 41.7; 28.3. MS *m/e*: 189 (8); 154 (9); 129 (5); 128 (31); 91 (35); 65 (11); 59 (23); 57 (100). IR (CCl_4): 3456; 3313 (ν C≡**C-H**); 1720. $[\alpha]^{21}_D$ = -10.6 (*c* = 1.01, $CHCl_3$). Anal. Calcd for $C_{15}H_{19}NO_2$: C 73.44; H 7.81; N 5.71. Found: C 73.36; H 7.84; N 5.73.

(S)-1-α-pyrrolidin-N-(t-butoxycarbonyl)-2-propynamine (**1e**)

224 mg (0.6 mmol) of (**6e**) were reacted following the general procedure for 45 min at -78°C. After workup 116 mg of crude were obtained which were purified by chromatography (SiO_2, eluent: CH_2Cl_2) to afford

49 mg (0.2 mmol) of pure (**1e**) as a pale yellow oil (yield 32%) and 56 mg (0.2 mmol) of (**7**) (37%). (**7**): ^{1}H-NMR (200 MHz) δ: 3.61 [m, 1H]; 3.3-3.2 [m, 1H]; 2.22 [bs, 1H]; 2.2-1.6 [m, 6H]; 1.47 [s, 9H], 1.5-1.1 [m, 4H], 0.90 (t, 3H, *J* = 6.6 Hz). MS *m/e*: 194 (27); 178 (12); 152 (6); 138 (78); 94 (100); 57 (89). (**1e**): ^{1}H-NMR (200 MHz) δ: 4.6-4.2 [m, 1H]; 3.6-3.2 [m, 1H+1H]; 2.21 [bs, 1H]; 2.1-1.9 [m, 4H]; 1.47 [s, 9H]. ^{13}C-NMR (50.3 MHz) d: 154.0; 79.7; 69.5; 54.3; 47.9; 31.9; 28.5; 22.7, 14.0. MS *m/e*: 195 (7); 194 (46); 178 (14); 139 (16); 138 (98); 95 (15); 94 (100); 57 (99). IR (CCl_4): 3313 (ν C≡**C-H**); 1693. $[\alpha]^{21}_D$ = -67.3 (*c* = 0.67, $CHCl_3$). Anal. Calcd for $C_{11}H_{17}NO_2$: C 67.66; H 8.78; N 7.17. Found: C 67.58; H 8.81; N 7.14.

(S)-1-[methyl-(3'-indolyl)]-N-(t-butoxycarbonyl)-2-propynamine (**1f**)

425 mg (1.0 mmol) of (**6f**) were reacted following the general procedure for 1 hour at -78°C. After workup 460 mg of crude were obtained which, after purification, (eluent: petroleum ether/ethyl acetate = 2/1) afforded 252 mg (0.9 mmol) of pure (**1f**) as a viscous yellow oil (yield 89%). (**1f**): ^{1}H-NMR (200 MHz) δ: 8.14 [bs, 1H]; 7.68 [d, 1H, *J* = 7.4 Hz]; 7.37 [d, 1H, *J* = 7.4 Hz]; 7.2-7.1 [m, 3H]; 4.9-4.7 [m, 1H+1H]; 3.2-3.1 [m, 2H]; 2.24 [s, 1H]; 1.42 [s, 9H]. ^{13}C-NMR (50.3 MHz) δ: 154.8; 136.0; 127.7; 123.3; 121.8; 119.3; 118.9; 111.1; 110.3; 83.6; 79.9; 71.5; 43.6; 31.4; 28.2. MS *m/e*: 284 (23); 229 (21); 228 (75); 211 (22); 168 (30); 167 (77); 131 (60); 129 (100); 103 (40); 102 (29); 77 (69); 57 (100). IR (CCl_4): 3489; 3457; 3313 (ν C≡**C-H**); 1720. $[\alpha]^{21}_D$ + 4.2 (*c* = 1.08, $CHCl_3$).

General procedure for the synthesis of chiral (1S, 2E)-3-tributylstannyl-N-(t-butoxy-carbonyl)-2-propenamine (**3**).

Tributyltincuprate was prepared according to the general route outlined by Lipshutz[17]. CuCN (1eq.) was suspended in THF, cooled at -78°C and treated with 1.6 M BuLi (2eq.) in hexane. The mixture was stirred for 15 min and then *n*-Bu_3SnH (2 eq.) was added dropwise. After 20 min at this temperature compound (**1f**) (1 eq.) was added and allowed to react to completion. The reaction mixture was then hydrolyzed with NH_4Cl/NH_4OH buffer solution at low temperature, extracted with Et_2O, then washed with brine and dried over Na_2SO_4. After solvent evaporation the obtained crude was purified by column chromatography.

(1S, 2E)-1-methyl-3-tributylstannyl-N-(t-butoxycarbonyl)-2-propenamine (**3a**)

99 mg (0.6 mmol) of (**1a**) were reacted for 1 hour following the general procedure. 570 mg of crude mixture were obtained which after purification (SiO_2, eluent: petroleum ether/ethyl acetate, gradient), afforded 196 mg (0.4 mmol) of (**3a**) as a colourless oil (yield 73%). (**3a**): ^{1}H-NMR (200 MHz) δ: 6.05 [dd, 1H, *J* = 19.0 Hz, *J* = 0.8 Hz]; 5.90 [dd, 1H, *J* = 19.0 Hz, *J* = 3.8 Hz]; 4.43 [bs, 1H]; 4.19 [m, 1H]; 1.6-1.2 [m, 12H]; 1.45 [s, 9H]; 1.23 [d, 3H, *J* = 6.6 Hz]; 1.0-0.7 [m,15H]. ^{13}C-NMR (75.45 MHz) δ: 155.2; 149.4; 126.1; 79.2; 50.3; 29.0; 28.4; 27.2; 20.8; 13.7; 11.6. MS *m/e*: 404 (36); 348 (68); 330 (13); 292 (50); 177; (53); 162 (19); 135 (30); 119 (57); 114 (47); 70 (48); 69 (58); 59 (93); 57 (100). $[\alpha]^{25}_D$ = - 29.9 (*c* = 0.98, $CHCl_3$).

(1S, 2E)-1-(1'-methyl)-ethyl-3-tributylstannyl-N-(t-butoxycarbonyl)-2-propenamine (**3b**)

300 mg (1.5 mmol) of (**1b**) were reacted for 1 hour following the general procedure. After workup and evaporation of the solvent 2.160 g of crude mixture were obtained in which (**3b**) and (**3'b**) were present in 90/10 ratio. Purification (SiO_2, eluent: petroleum ether/ethyl acetate = 20:1) afforded 536 mg (1.1 mmol) of pure (**3b**) as a colourless oil (yield 73%). (**3b**): ^{1}H-NMR (200 MHz) δ: 6.04 [dd, 1H, *J* = 19.1 Hz, *J* = 1.4 Hz]; 5.84 [dd, 1H, *J* = 19.1 Hz, *J* = 4.6 Hz]; 4.43 [bs, 1H]; 4.3-4.1 [m, 1H]; 1.9-1.7 [m, 1H]; 1.5-1.2 [m, 12H]; 1.44 [s, 9H]; 1.2-0.7 [m, 15H+6H] ^{13}C-NMR (50.3 MHz) δ: 155.3; 146.7; 127.6; 78.9; 60.2; 32.2; 29.0; 28.3; 27.3; 18.7, 17.8; 13.6; 9.4. MS *m/e*: 432 (13); 376 (39); 179 (20); 177 (23); 135 (25); 121 (23); 85 (36); 83 (61); 57 (100). $[\alpha]^{25}_D$ = -14.5 (*c* = 1.04, $CHCl_3$).

(1S,2E)-1-(1'-methyl)-propyl-3-tributylstannyl-N-(t-butoxycarbonyl)-2-propenamine (**3c**)

250 mg (1.2 mmol) di (**1c**) were reacted for one hour following the general procedure. After workup and evaporation of the solvent 1.165 g of crude mixture were obtained in which (**3c**) and (**3'c**) were recovered in 95/5 ratio. 970 mg of this material were purified by column chromatography (Florisil, eluent: petroleum ether/ethyl acetate, gradient) affording 296 mg (0.6 mmol) of pure (**3c**) as a colourless oil (yield 59%). (**3c**): ^{1}H-NMR (200 MHz) δ: 6.04 [dd, 1H, *J* = 18.9 Hz, *J* = 1.1 Hz]; 5.82 [dd, 1H, *J* = 18.9 Hz, *J* = 4.8 Hz]; 4.56 [m, 1H]; 4.08 [m, 1H]; 1.6-1.2 [m, 12H+2H+1H]; 1.45 [s, 9H]; 0.9-0.8 [m, 15H + 6H]. ^{13}C-NMR (50.3 MHz)

(APT) δ: 156.1; 146.8; 128.5; 79.6; 59.8; 39.5; 29.6; 28.9; 27.7; 25.8; 15.6; 14.2; 12.3; 10.0. MS *m/e*: 446 (8); 390 (35); 334 (12); 332 (10); 177 (14); 176 (10); 59 (24); 57 (100). $[\alpha]^{20}_D$ = - 11.2 (*c* = 1.02, $CHCl_3$).

(1S, 2E)-1-benzyl-3-tributylstannyl-N-(t-butoxycarbonyl)-2-propenamine (**3d**)

803 mg (3.3 mmol) of (**1d**) were reacted for one hour following the general procedure. After workup and evaporation of the solvent 3.664 g of crude mixture were obtained which after purification (Florisil, eluent: petroleum ether (30°-50°)/ethyl ether, gradient) afforded 1.569 g (2.9 mmol) of (**3d**) as a pure colourless oil (yield 88%). (**3d**): ^{1}H-NMR (200 MHz) δ: 7.3-7.1 [m, 5H]; 6.01 [d, 1H, *J* = 19.0 Hz]; 5.89 [dd, 1H, *J* = 19.0 Hz, *J* = 3.4 Hz]; 4.6-4.3 [m, 1H+1H]; 2.84 [d, 2H, *J* = 6.0 Hz]; 1.6-1.2 [m, 12H]; 1.41 [s, 9H]; 0.9-0.6 [m, 15H]. ^{13}C-NMR.(75.45 MHz) δ: 155.2; 147.1; 137.6; 129.6, 128.1, 127.7; 126.3; 79.2; 55.8; 41.6; 29.0; 28.3; 27.2; 13.7; 9.4. MS *m/e*: 404 (5); 178 (7); 132 (11); 130 (13); 122 (17); 92 (100); 87 (19); 85 (31); 66 (11); 60 (38); 58 (31); 57 (19). $[\alpha]^{20}_D$ = - 5.9 (*c* = 1.00, $CHCl_3$).

(1S, 2E)-1-α-pyrrolidin-3-tributylstannyl-N-(t-butoxycarbonyl)-2-propenamine (**3e**)

24 mg (0.1 mmol) of (**1e**) were reacted for 20 min following the general procedure. After workup and evaporation of the solvent 85 mg of crude were obtained in which (**3e**) e (**3'e**) were recovered in 90/10 ratio. After purification (Florisil, eluent: petroleum ether/ethyl acetate, gradient) 34 mg (0.07 mmol) of pure (**3e**) were obtained as a colourless oil (58%). (**3e**): ^{1}H-NMR (200 MHz) δ: 5.92 [d, 1H, *J* = 19.0 Hz]; 5.80 [dd, 1H, *J* = 19.0 Hz, *J* = 3.8 Hz]; 4.3-4.2 [m, 1H]; 3.39 [bt, 2H]; 2.2-1.6 [m, 4H]; 1.6-1.2 [m, 12H]; 1.42 [s, 9H]; 0.9-0.8 [m, 15H]. ^{13}C-NMR (75.45 MHz) δ: 154.9; 148.4; 125.6; 78.9; 61.7; 54.4; 46.4; 45.2; 29.1; 28.4; 27.2; 13.7; 9.4. MS *m/e*: 430 (41); 374 (100); 318 (15) 177(28); 95 (38) 57 (100). $[\alpha]^{20}_D$ = -50.5 (*c* = 0.61 $CHCl_3$).

(1S, 2E)-1-[methyl-(3-indolyl)]-3-tributylstannyl-N-(t-butoxycarbonyl)-2-propenamine (**3f**)

102 mg (0.4 mmol) of (**1f**) were reacted for one hour following the general procedure. After workup and evaporation of the solvent 304 mg of crude mixture were obtained which, after purification (Florisil, eluent: petroleum ether/ethyl acetate = 7:1), afforded 144 mg (0.25 mmol) of (**3f**) as a colourless oil (yield 69%). (**3f**): ^{1}H-NMR (200 MHz) δ: 8.03 [bs, 1H]; 7.63 [bd, 1H, *J* = 7.1 Hz]; 7.4-7.3 [m, 1H]; 7.2-6.8 [m, 3H]; 6.06 [d, 1H, *J* = 19.2 Hz]; 5.94 [dd, 1H, *J* = 19.2 Hz, *J* = 3.0 Hz]; 4.7-4.4 [bm, 1H+1H]; 3.1-2.9 [m, 2H]; 1.5-1.2 [m, 12H]; 1.41 [s, 9H]; 1.0-0.8 [m,15H]. ^{13}C-NMR (75.45 MHz) δ: 155.4; 148.0; 136.1; 128.0; 122.6; 121.8; 119.3; 118.8; 112.0; 110.9; 79.1; 55.3; 31.0; 29.0; 28.3; 27.2; 13.6; 11.6. MS *m/e*: 519 (2); 460 (2); 177 (11); 168 (14); 130 (100); 83 (18); 59 (15); 57 (42). $[\alpha]^{25}_D$= -2.8 (*c* = 1.15, $CHCl_3$).

General procedure for the synthesis of the Mosher's amides of (**8-a,b,d,f**) *and* (**9-c,d**).

The *t*-Boc protected amines (**1-c,d**) or (**3 a,b,d,f**) (0.1 mmol) were dissolved in $CHCl_3$ and stirred under nitrogen with $(CH_3)_3SiI$ (0.12 mmol) for 10 minutes. The reaction was then stopped by dilution with methanol and after evaporation of the solvent the corresponding deprotected propargylamines (**9c**)-(**9d**) and allylamines (**8a**)-(**8b**)-(**8d**)-(**8f**) were recovered in the crude by ^{1}H NMR analysis. The obtained material was dissolved in CCl_4 (1 mL) and reacted for 48 hours with a solution of 25 mg (0.1 mmol) of (*S*)-(+)-MTPA-Cl in 1 mL of pyridine. After dilution with water and extraction with ether, the organic phase was washed several times with a concentrated solution of Na_2CO_3 and then dried over Na_2SO_4. After evaporation of the solvent the crude was analyzed by ^{1}H NMR and the enantiomeric excess was determined. After purification by column chromatography and ^{1}H NMR analysis no variation of the enantiomeric excess was observed.

(1S, 2E)-1-methyl-3-phenyl-N-(t-butoxycarbonyl)-2-propenamine (**10**)

256 mg (0.6 mmol) of (**3a**) were dissolved with benzene (1 mL), and reacted with 110 mL of bromobenzene (1.0 mmol) and with a catalytic amount (3%) of $Pd(PPh_3)_4$. The reaction was left at 80°C for 48 hours and then filtered on SiO_2 (6 cm, eluent Et_2O). The organic layer was washed with water, then stirred for 30 min with a KF saturated solution. After filtration, evaporation of the solvent and purification by column chromatography (SiO_2, 18 cm, eluent: petroleum ether/ethyl acetate = 3/1) 86 mg (0.3 mmol) of pure (**10**) were obtained as a white low melting solid (yield 63%). (**10**): ^{1}H-NMR (200 MHz) δ: 7.4-7.2 [m, 5H]; 6.49 [dd, 1H, *J* = 16.0 Hz, *J* = 1.2 Hz]; 6.15 [dd, 1H, *J* = 16.0 Hz, *J* = 5.7 Hz]; 4.57 [m, 1H]; 4.39 [m, 1H]; 1.46 [s, 9H]; 1.3 [d, 3H, *J* = 6.6 Hz]. ^{13}C-NMR (75.45 MHz) δ: 155.1; 136.7; 131.7; 129.1; 128.5; 127.4; 126.3; 79.3; 47.9; 28.4;

21.1. MS *m/e*: 191 (29); 176 (14); 146 (39); 132(18); 131(38); 130 (100); 129 (17); 115 (41); 91 (12); 57 (25). $[\alpha]^{22}_D$= -60.9 (*c* = 1.08, $CHCl_3$). Anal. Calcd. for $C_{15}H_{21}NO_2$: C 72.84; H 8.56; N 5.66. Found: C 72.78; H 8.53; N 5.64.

(1S, 2E)-1-methyl-3-(2-pyridyl)-N-(t-butoxycarbonyl)-2-propenamine (**11**)

210 mg (0.5 mmol) of (**3a**) were dissolved in benzene (1 mL), and reacted with 70 mL of 2-bromopyridine (0.7 mmol) and with a catalytic amount (3%) of $Pd(PPh_3)_4$. The reaction was left at 80°C for 40 hours and then filtered on SiO_2 (6 cm, eluent Et_2O). The organic layer was washed with water, then stirred for 30 min with a KF saturated solution. After filtration, evaporation of the solvent and purification by column chromatography (SiO_2, 18 cm, eluent: petroleum ether/ethyl acetate = 3/1) 68 mg (0.3 mmol) of pure (**11**) were obtained as a white low melting solid (yield 60%). (**11**): ^{1}H-NMR (200 MHz) δ: 8.52 [ddd, 1H, *J* = 4.8 Hz, *J* = 1.8 Hz, *J* = 1.2 Hz]; 7.60 [t, 1H, *J* = 7.6 Hz]; 7.24 [d, 1H, *J* = 7.6 Hz]; 7.10 [ddd, 1H, *J* =7.6 Hz, *J* = 4.8 Hz, *J* = 1.0 Hz]; 6.68 [dd, 1H, *J* = 15.8 Hz, *J* = 4.7 Hz]; 6.55 [d, 1H, *J* = 15.8 Hz]; 4.60 [bs , 1H], 4.46 [m, 1H]; 1.44 [s, 9H]; 1.31 [d, 3H, *J* = 6.6 Hz];. ^{13}C-NMR.(75.45 MHz) δ: 153.2; 153.1; 147.4; 134.4; 134.3; 126.8; 120.1; 119.7; 77.4; 45.5; 26.3; 19.0. MS *m/e*: 192 (23); 148 (25); 147 (21); 133(21); 132 (37) 131(31); 130 (21); 117 (32); 106 (100); 78 (13); 57 (55). $[\alpha]^{24}_D$= -60.9 (*c* = 1.12, $CHCl_3$). Anal. Calcd. for $C_{14}H_{20}N_2O_2$: C 67.72; H 8.12; N 11.28. Found: C 67.65; H 8.09; N 11.32.

(1S, 2E, 5E)-1-methyl-6-phenyl-N-(t-butoxycarbonyl)-2,5-esadienamine (**12**)

210 mg (0.5 mmol) of (**3a**) were dissolved with DMF (2 mL), and reacted with 85 mL of cinnamylacetate (0.5 mmol), with 64 mg (1.5 mmol) of LiCl and with a catalytic amount (3%) of $Pd_2(dba)_3$. The reaction was left at room temperature for 24 hours and then hydrolyzed with water and extracted with ether. The organic phase was washed twice with a saturated solution of KF in ammonia (10%) and then with brine. After evaporation of the solvent and purification by chromatography (eluent: CH_2Cl_2/Et_2O = 20/1) 89 mg (0.3 mmol) of pure (**12**) were obtained as a pale yellow oil (yield 68%). (**12**): ^{1}H-NMR (200 MHz) δ: 7.38-7.19 [m, 5H]; 6.39 [d, 1H, *J* = 16.2 Hz]; 6.19 [dt, 1H, *J* = 16.2 Hz, *J* = 6.3 Hz]; 5.66 [dt, 1H, *J* =15.6 Hz, *J* = 6.3 Hz]; 5.48 [dd, 1H, *J* = 15.6 Hz, *J* = 5.2 Hz]; 4.42 [bs, 1H]; 4.21 [m , 1H], 2.92 [t, 2H, *J* = 6.3 Hz]; 1.44 [s, 9H]; 1.21 [d, 3H, *J* = 6.6 Hz];. ^{13}C-NMR (75.45 MHz) δ: 155.3; 143.3; 137.5; 133.2; 130.7; 128.4; 127.6; 127.0; 126.0; 79.2; 47.6; 35.4; 28.4; 21.1. MS *m/e*: 231 (9); 170 (100); 144 (47); 143 (42); 142 (13); 141 (16); 128 (39) 127 (32); 117 (13); 116 (11); 115 (61); 96 (12); 91 (53); 88 (95); 57 (30). $[\alpha]^{26}_D$ = -30.6 (*c* = 1.05, $CHCl_3$). Anal. Calcd. for $C_{18}H_{25}NO_2$: C 75.22; H 8.77; N 4.87. Found: C 75.15; H 8.75; N 4.88.

(1S, 2E)-1-methyl-3-iodo-N-(t-butoxycarbonyl)-2-propenamine (**13**)

232 mg (0.8 mmol) of (**3a**) were dissolved in $CHCl_3$ (1 mL), and reacted with a solution of 211 mg (0.8 mmol) of I_2 in 1 mL of $CHCl_3$. The reaction was left at room temperature for 3 hours and then filtered on SiO_2. After chromatography (eluent: CH_2Cl_2/Et_2O = 20/1) 123 mg (0.4 mmol) of pure (**13**) were obtained as a white solid (yield 71%). (**13**): ^{1}H-NMR (200 MHz) δ: 6.49 [dd, 1H, *J* = 14.5 Hz, *J* = 5.8 Hz]; 6.25 [dd, 1H, *J* = 14.5 Hz, *J* = 1.1 Hz]; 4.45 [bs, 1H]; 4.20 [m, 1H]; 1.43 [s, 9H]; 1.20 [d, 3H, *J* = 7.0 Hz]. ^{13}C-NMR (75.45 MHz) δ: 154.8; 147.4; 79.7; 76.5; 50.4; 28.3; 20.2. MS *m/e*: 241 (21); 181 (27); 114 (100); 113 (38); 70 (16); 59 (12); 57 (49). $[\alpha]^{22}_D$= -55.3 (*c* = 1.06, $CHCl_3$).

(1S, 2E, 4E, 6S)-1-methyl-6-(1'-methyl)-ethyl-N,N'-(di-t-butoxycarbonyl)-2,4-hexadien-1,6-diamine (**14**).

58 mg (0.2 mmol) of (**13**) were dissolved in DMF (1 mL) and with 5 mg of $PdCl_2(CH_3CN)_2$ (0.02 mmol). 114 mg (0.2 mmol) of (**3b**) were dissolved with DMF (2 mL), added to the rection mixture and left at room temperature with magnetic stirring for 50 hours. After this time the reaction was diluted with water and then extracted with ether. The organic layer was washed with brine. Evaporation of the solvent gave 253 mg of crude which was purified by chromatography (eluent: petroleum ether/ethyl acetate = 5/1) affording 39 mg (0.1 mmol) of pure (**14**) as a pale yellow oil (yield 54%). (**14**): ^{1}H-NMR (200 MHz) δ: 6.2-6.0 [m, 1H+1H]; 5.7-5.4 [m, 1H+1H]; 4.48 [m, 1H+1H]; 4.23 [m, 1H]; 3.98 [m, 1H]; 1.43 [s, 9H+9H]; 1.74 [m , 1H], 1.2 [d, 3H, *J* = 6.6 Hz]; 0.88 [d, 3H, *J* = 7.0 Hz]; 0.87 [d, 3H, *J* = 7.0 Hz]. ^{13}C-NMR (75.45 MHz) δ: 156.0; 155.56; 135.4; 133.1; 130.7; 129.3; 79.8; 57.8; 48.3; 33.1; 28.9; 21.5; 19.2; 18.7. MS *m/e*: 256 (3); 212 (13); 195 (10); 169 (15); 152 (22); 126 (29); 124 (21) 108 (55); 82 (51); 57 (100). $[\alpha]^{24}_D$= -25.7 (*c* = 1.08, $CHCl_3$). Anal. Calcd. for $C_{20}H_{36}N_2O_4$: C 65.19; H 9.85; N 7.60. Found: C 65.24; H 9.89; N 7.57.

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